HFA-305, Division of Dockets Management

Date of Approval: SEP 15 2004

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-247

OXYTETRACYCLINE HCL SOLUBLE POWDER-343

oxytetracycline hydrochloride

To add a claim for the skeletal marking of finfish fry and fingerlings

Sponsored by:

Phoenix Scientific, Inc.

2004-200-247

FOIS 1

2. *EFFECTIVENESS:*

A combination of data from many different fish species reared in different temperatures and management systems were used to support the determination of effectiveness in all teleost (bony) fish, consistent with the *Guidance for Industry: FDA Approval of Animal Drugs for Minor Uses and for Minor Species* (FDA/CVM January *1999).* The data summarized in this section are publicly available data contained in Public Master File 005667 which were compiled under National Research Support Project-7, a national agricultural research program for obtaining clearances for use of new drugs in minor species and for special uses. The range of oxytetracycline concentrations, 200 to 700 mg OTC/L of water, is supported by the studies summarized in this section, as well as the literature references at the end of this section.

a. Dosage Characterization:

Reports of successful marking of bony structures of fish, especially the otoliths, have been published for decades. There is a significant body of evidence that tetracyclines stain bony tissues in a wide range of species. The process of marking bony structures with tetracyclines was described in the literature as early as 1962. The literature reflects the widespread use of oxytetracycline by various routes and demonstrates the breadth and number of available publications on marking. This literature provided information to demonstrate the safety and effectiveness of oxytetracycline marking of finfish.

The otolith was selected for evaluation of marking success because otoliths are the first permanent calcified structures present in the earliest life stages of fish and are, effectively, biological internal tags. Once deposited, calcium in the otolith was mobilized little if at all.

Immersion was chosen as the route of administration because immersion marking allows fish to be mass marked with minimal handling. The doses selected were based on the doses found in the published literature.

b. Substantial Evidence:

1. Field Study

   Type of Study: Clinical Field Trial

   Name and Address of Investigator: W. Jenkins
   South Carolina Department of Natural Resources
   Charleston, SC

   General Design of the Study:

   a. Purpose of the Study: To evaluate the effectiveness of using oxytetracycline (OTC) to mark red drum fingerlings for later identification as stocked fish in wild populations.

b. Test Animals: Red drum fingerlings *(Sciaenops ocellatus)*

c. Treatment Groups: This study included only one treatment group, oxytetracycline-treated fish.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosage Used: 500 mg oxytetracycline/L of water for 4 hours

g. Test Duration: 30 days (treatment to examination)

h. Variables: Examination of otoliths to identify marks and mortality associated with OTC immersion marking

Methods: Red drum were harvested from 5 ponds in the fall of 1996 and 4 ponds in the spring of 1997 for immersion treatment. Fish were placed in a holding tank and acclimated to 15 ppt salinity water. OTC was added to the tank to provide a 500 mg/L OTC concentration. Fish were held for 4 hours. Fish were then transferred to a hauling trailer filled with 15 ppt salinity water. Fish were restocked in a pond at the culture facility and held for 7 days. The salinity in the pond was raised to the concentration of the area to be stocked during the 7-day holding period. Fish were harvested and transported to stocking sites for release. **A** subsample of each group of marked fish was retained for 30 days to confirm mark effectiveness.

Results: Visible marks could be detected on otoliths in all batches of treated fish. Samples of fish from the wild population indicated that up to 40% of stocked age one year fish had OTC otolith marks.

Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith is a four-hour immersion at 500 mg/L oxytetracycline hydrochloride.

2. Field Study

Type of Study: Clinical Field Trial

Name and Address of Investigator: M. L. Hendricks
Pennsylvania Fish & Boat Commission
State College, PA

General Design of the Study:

a. Purpose of the Study: To apply unique multiple marks needed to discriminate between groups of fish from different egg source rivers, fish released as fry or fingerlings, and fish released at different sites.

b. Test Animals: American shad fry *(Alosa sapidissima)*, 3-15 days old

c. Treatment Groups: Six different single and multiple marks were applied. A total of 8,500,000 fry were produced with all except 13,500 stocked in the Susquehanna River and its tributaries, or the Lehigh River. Fry were marked in 1200 L rearing tanks (40 total), each containing up to 500,000 fry.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosage Used: 256 mg oxytetracycline (buffered)/L of water for 4 hours

g. Variable: Fry from 6 tanks and raceways were sampled for otolith mark retention.

Results: Retention of immersion marks for American shad fry was 100% for all production groups in 1996. Refer to the following table.

Table 2.1. Oxytetracycline mark retention for American shad reared in 1996.

Tank/ Raceway	Mark Applied (day)	Marks Visualized (day)	Number Examined	Number Marked	Number stocked
Race F1	9,12,15	9,12,15	19	19	171,700
Race F3	3,9,12,15	3,9,12,15	19	19	277,100
Race E1	3,6,9	3,6,9	18	18	42,900
Race F2	3,9,12	3,9,12	19	19	561,100
Race F4	3,6,9,12	3,6,9,12	19	19	682,500
Not Sampled	3	3			5,730,200
Tank J4*	3	3	17	17	Not stocked

*Sampled at 28 days of age.

All fry produced received marks.

Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith is a four-hour immersion at 256 mg/L oxytetracycline hydrochloride.

3. Field Study

Type of Study: Clinical Field Trial

Name and Address of Investigator: K. D. Cottrell
Illinois Department of Conservation
Springfield, Illinois

General Design of the Investigation:

a. Purpose of the Study: To determine the effectiveness of oxytetracycline HCl in the marking of otoliths of fry and fingerling fish of different species.

b. Test Animals and Treatment Groups: Largemouth bass *(Micropterus salmoides)* fingerlings, walleye *(Stizostedion vitreum)* fry and fingerlings, and sauger *(Stizostedion canadense)* fry and fingerlings.

C. Treatment Groups: The fish were assigned to either treatment (500 mg/L for 6 hours) or smaller control groups.

Table 2.2. Number of each fish species treated during 1997.

Species	Treated	Control
Largemouth bass fingerlings	25,000	300
Walleye fry	5,837,400	100,000
Walleye fingerlings	143,306	1,000
Sauger fry	2,400,000	100,000
Sauger fingerlings	166,934	1,000

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: 0 and 500 mg oxytetracycline/L of water for 6 hours

g. Test Duration: 30 to 45 days (from treatment to sampling)

h. Variables: Clinical observations and examination of otoliths to identify marks (50 fish from each treated group, and 50 from each control group).

Methods:

Fry – Groups of 100,000 fry were placed in a 500 mg/L concentration of oxytetracycline in **3** gallons of water within a plastic fish hauling bag for six hours. To ascertain mark retention, 100,000 of the marked and control **fry** were placed into separate rearing ponds. At the end of the rearing period (45 days for walleye and 60 days for sauger), samples of 50 fish per group were collected at harvest and checked for mark effectiveness.

Fingerlings – Fish were immersed in a 500 mg/L concentration of oxytetracycline for six hours. Marked and control fish were retained for 30 days post-treatment and then harvested for examination. Samples of at least 50 fish from each group were checked for mark effectiveness.

Results: Results are shown in the following table.

Table 2.3. Results of otolith marking field effectiveness trials in 1997.

Species	Treatment	Number Examined	Number Marked	Percent Marked
Walleye fry	OTC Immersion	50	50	100
	Control	50	7	14
Walleye fingerlings	OTC Immersion	50	100	100
	Control	50	0	0
Sauger fingerlings	OTC Immersion	50	50	100
	Control	50	0	0
Sauger fry	OTC Immersion	50	50	100
	Control	50	0	0
Largemouth bass fingerlings	OTC Immersion	50	50	100
	Control	50	0	0

Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otoliths of walleye fry and fingerlings, sauger fry and fingerlings, and largemouth bass fingerlings is a six-hour immersion in 500 mg/L oxytetracycline hydrochloride.

4. Field Study

Type of Study: Clinical Field Trial

Name and Address of Investigator: D. O. Lucchesi
South Dakota Department of Game, Fish, and Parks
Pierre, South Dakota

General Design of the Study:

a. Purpose of the Study: To determine the effectiveness of oxytetracycline HCl in the marking of otoliths of walleye fry and fingerlings.

b. Test Animals: Walleye ***(Stizostedion vitreum)*** fry and fingerlings.

Table 2.4. Fish treated during a field study.

Species	Number of Fish
Walleye fry	12,000,000
Walleye fingerlings	150,000

c. Treatment Groups: Natural rearing ponds were stocked with either 500 mg/L or 700 mg/L marked fry, or 500 mg/L marked fingerlings. Two ponds were stocked with 500 mg/L marked fry and two ponds were stocked with 700 mg/L marked fry. Equal numbers of marked and unmarked fry were stocked into 0.8 ha hatchery ponds to compare survival.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride.

e. Route of Administration: Immersion (bath).

f. Dosages Used: Walleye fry were marked at either 500 mg/L or 700 mg/L. Walleye fingerlings were marked at 500 mg/L. Immersion was for 6 hours.

g. Test Duration: 30 days to 3 months (from treatment to sampling).

h. Variables: Examination of otoliths to identify marks and mortality associated with OTC immersion marking

Methods:

To produce the marking bath, an OTC slurry was mixed in a 20 L plastic bucket and was then buffered to a neutral pH using sodium phosphate (dibasic, Na_2HPO_4). Walleye fry were immersed for **6** hours in 683 liter fiberglass raceways containing either 500 or 700 mg OTC/L. Density of fry did not exceed 2,000 fry per liter. Pond-reared fingerlings were marked by immersion for 6 hours in a 500 mg OTC/L water solution in 632 liter fiberglass transfer tanks. Fingerling densities did not exceed 50 fish per liter.

To evaluate marking effectiveness and mark retention, OTC-marked fry and fingerlings were stocked into natural rearing ponds that had complete fish kills the previous winter. These test ponds contained marked individuals from one of three test groups: fry immersed in 500 rng OTC/L or 700 mg OTC/L, or fingerlings immersed in 500 mg/L. Test ponds were electrofished in early fall (approximately **3** months after marking) to recover walleye for evaluation of the mark quality.

To evaluate mortality associated with OTC immersion marking, the 0.8 ha ponds were seined approximately 30-40 days after stocking. **A** sample of 100 fingerlings per pond was examined for OTC otolith marks.

Results: Results are shown in the following table.

Table 2.5. Visibility of walleye otolith marks **3** months after marking as fry.

OTC Concentration (mg/L)	Mark Intensity			
	0	**1**	**2**	**3**
500"	50%	**40%**	10%	**0**
700[a]	0	0	18%	82%
700[b]	0	0	2%	98%

"1996 [b]1997

These findings suggest that better quality marks are obtained when fish are immersed in a bath containing 700 mg/L OTC. Problems with OTC precipitating out of solution typically occurred at a pH of higher than 8.0. Therefore, the pH of the bath was maintained at 7.0 to 7.6, even when hatchery water pH exceeded that range.

Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith of walleye fry is a six-hour immersion at 700 mg/L OTC.

SUPPORTING LITERATURE

The following published articles were submitted to support the effectiveness of oxytetracycline for the marking of otoliths in bony fish:

1. Brooks, R.C., R.C. Heidinger, and C.C. Kohler. Mass-Marking Otoliths of Larval and Juvenile Walleyes by Immersion in Oxytetracycline, Calcein, or Calcein Blue. North American Journal of Fisheries Management 14: 43-150, 1994.

2. Hendricks, M.L., T.R. Bender, and V.A. Mudrak. Multiple Marking of American Shad Otoliths with Tetracycline Antibiotics. North American Journal of Fisheries Management, 11:2 12-219, 1991.

3. Secor, D.H., M.G White, and J.M Dean. Immersion Marking of Larval and Juvenile Hatchery-Produced Striped Bass with Oxytetracycline. Transactions of the American Fisheries Society, 120:26 1-266, 1991.

4. Thomas, L.M. Chemical Mark Application in Red Drum *(Sciaenops ocellatus).* Thesis for Master of Science at Corpus Christi State University, Corpus Christi, Texas. 44 pages, 1993.

5. Younk, **J.A.** and M.F. Cook. Fluorescent Chemical Marking of Walleye Larvae with a Selected Literature Review of Similar Investigations. Minnesota Department of Natural Resources Investigational Report 408. 18 pages, 1991.

2. ***TARGETANIMAL SAFETY:***

The data summarized in this section is publicly available data contained in Public Master File 005667 which were compiled under National Research Support Project-7, a national agricultural research program for obtaining clearances for use of new drugs in minor species and for special used.

a. "Toxicity of Oxytetracycline and Calcein to Juvenile Striped Bass."

1. Type of Study: Target animal safety

2. Name and Address of Investigators: B.W. Bumguardner and T.L. King
Texas Parks and Wildlife Department
Palacios, Texas

3. General Design of the Study:

a. Purpose of the Study: The study was designed to identify adverse effects of exposing fish to a geometric sequence of oxytetracycline by immersion.

b. Test Animals: Juvenile striped bass (*Morone saxatilis*), approximately 48 mm total length and 2.2 g.

c. Treatment Groups: Three replicates per concentration were tested with ten fish per replicate. The first set of tests included 6 different OTC concentrations. The second set of tests included **3** higher concentrations.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: Concentrations of 0, 55.8, 111.6, 223.3, 446.5, and 893 mg/L; second set of tests: 893, 1786, and 3572 mg/L. 6-hour immersion exposure.

g. Test Duration: 26 days (from set **up** to final observations)

h. Variables: Survival and behavior at 1 hour intervals during the 6-hour treatment and for 6 hours after treatment were observered. Mortality was monitored daily for the next 4 days. Water conditions were also monitored for temperature, salinity, pH, and total hardness.

4. Methods:

After a 22-day acclimation period in **a** recirculating raceway, the fish were transferred to the test chambers. The test chambers were 4.5 liter aquaria containing salt water (enough to make the total volume 2 liters after addition of OTC solution). OTC HCl unbuffered solution was added to provide concentrations of 0, 55.8, 111.6, 223.3, 446.5, and 893 mg/L. Since no deaths were seen, the 893 mg/L concentration was repeated and 1786 and 3572 mg/L concentrations were added. Fish were immersed for ***6*** hours. Fish were then

placed in a beaker while the aquaria were rinsed. Fish were then placed back into aquaria. Water was exchanged every 24 hrs for 4 days.

5. Results:

a. Water conditions: Water conditions are included in the following table.

Table 3.1. Water conditions during a study to evaluate the safety of oxytetracycline solutions with juvenile striped bass.

Condition	Pre Treatment	During Treatment
Temperature	26°C	26°C
Salinity	5 ± 1.9%	7%
pH	8.3	3.25-8.56*
Total hardness		33.4 mg/L (as CaCO3)

*pH varied depending on OTC concentration

A white precipitate was observed in the higher OTC concentration test chambers.

b. Mean Mortality: Percent mean mortality results are included in the following table.

Table 3.2. Mean mortality (%) results of a study to evaluate the safety of calcein and oxytetracycline solutions with juvenile striped bass.

Concentration	During Treatment	After Treatment	Total (and range)
0 (control)	*0*	6.7	6.7 (0-10)
55.8 mg/L	0	*0*	*0*
111.6 mg/L	*0*	0	0
223.3 mg/L	0	0	0
446.5 mg/L	0	30	30 (10-60)
893 mg/L	0	81.7	81.7 (60-100)
1786 mg/L	23.3	73.3	96.7 (90-100)
3572 mg/L	100		100

Stressed behavior (rapid swimming at the water's surface) was reported in concentrations of OTC 446.5 mg/L and higher.

6. Conclusion: The pH of the immersion solution may have caused or contributed to the death of the fish in the highest dose groups. The mean pH of test aquaria water after addition of OTC solution began to decrease significantly at 893 mg OTC/L. At 1786 mg/L, the pH was more than 1.5 units lower than that of the control group; at 3572 mg/L, the pH was more than 5 units lower than that of the control group.

Water quality, especially pH, must be monitored and controlled when using higher concentrations of OTC for immersion of fish. Buffering of the water can be done to maintain a healthy pH when OTC is used.

b. Field Study

1. Type of Study: Clinical Field Trial

2. Name and Address of Investigator: W. Jenkins
South Carolina Department of Natural Resources
Charleston, SC

3. General Design of the Study:

a. Purpose of the Study: This study was primarily designed to demonstrate effectiveness. During the fall of 1996 and spring of 1997, fish were stocked in hatchery ponds following treatment. The ponds were harvested approximately one week later to evaluate post-treatment mortality.

b. Test Animals: Red drum *(Scianenops ocellatus)* fingerlings.

C Treatment Group: This study included only one treatment group, oxytetracycline-treated fish.

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: 500 mg oxytetracycline/L for 4 hours

g. Test Duration: Approximately one week (treatment to harvest)

h. Variables: Mortality occurring one week following treatment was recorded.

4. Methods: Red drum fingerlings were placed in a holding tank on a trailer and acclimated to approximately 15 ppt salinity. Adequate OTC was added to provide a 500 mg/L concentration. Fish were held for 4 hours and then transferred to a hauling trailer. Fish were stocked in a pond at the culture facility and held for one week. During that week pond salinity was slowly raised to the same concentration as the area to be stocked (29-30 ppt). Fish were then harvested and transported to stocking sites for release.

5. Results: Results are included in the following table.

Table 3.3. Mean size and survival of red drum fingerlings treated from 9/96-5/97 with OTC at a concentration of 500 mg/L for 4 hours.

Treatment Date	Mean Length (mm)	Mean Weight (g)	Number of Fish Treated	(%)	Number Harvested
9/16	39	0.59	37,047	72.2	26,746
10/15	37	0.67	63,898	43.1	28,061[a]
10/16	25	0.21	381,028	66.6	253,637
10/22	37	0.68	43,332	71.1	30,801
11/7	13	0.10	265,593	86.4	229,712[b]
5/15	33	0.36	65,810	82.8	54,474
5/22	28	0.25	114,423	80.7	92,395
5/27	29	0.24	470,611	86.8	408,653
5/29	34	0.31	143,589	93.9	134,900

[a]This pond had a dense growth of macrophytic algae. Fish got stranded in the algal mat during harvest.
[b]A salinity acclimation error during post-treatment resulted in 20% mortality during harvest and release, therefore only 183,770 fish were released alive.

6. Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith, a four-hour immersion in 500 mg/L oxytetracycline, is safe to red drum fingerlings.

c. Field Study

1. Type of Study: Clinical Field Trial

2. Name and Address of Investigator: K. D. Cottrell
Illinois Department of Conservation
Springfield, Illinois

3. General Design of the Study:

a. Purpose of the Study: The studies were primarily designed to demonstrate effectiveness. The studies involved the treatment of many species and large numbers of fish. The studies demonstrate several issues related to target animal safety.

b. Test Animals: Largemouth bass ***(Micropterus salmoides)*** fingerlings, walleye ***(Stizostedion vitreum)*** fry and fingerlings, and sauger ***(Stizostedion canadense)*** fry and fingerlings.

c. Treatment Groups: The fish were assigned to either treatment (500 mg/L for 6 hours) or smaller control groups according to the following table.

Table 3.4. Treatment groups for a marking study conducted in 1997.

Species	Treatment (number)	Control (Number)
Largemouth bass fingerlings	25,000	300
Walleye fry	5,837,400	100,000
Walleye fingerlings	143,306	1,000
Sauger fry	2,400,000	100,000
Sauger fingerlings	166,934	1,000

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: 0 and 500 mg oxytetracycline/L of water for 6 hours

g. Test Duration: 1 day (fish stocked the day of treatment)

h. Variables: Mortality and adverse reactions were recorded.

4. Methods:

Fry - Groups of 100,000 fry were placed in a 500 mg/L concentration of oxytetracycline in 3 gallons of water within a plastic fish hauling bag for six hours.

Fingerlings - Fish were immersed in a 500 mg/L concentration of oxytetracycline for six hours.

5. Results: Results are included in the following table.

Table 3.5. Mortality and adverse reactions observed in 1997 at Jake Wolf, Little Grassy and LaSalle Hatcheries in Illinois.

Species	Number Treated	Mortalities	Adverse Reactions
Largemouth bass fingerlings	25,000	0	None
Walleye fry	5,824,080	0	None
Walleye fingerlings	138,626	0	None
Sauger fry	22,000,000	0	None
Sauger fingerlings	166,934	0	None

No adverse reactions or mortality occurred in control groups in any of the species treated.

6. Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith, a six-hour immersion at 500 mg/L, is safe to fry and fingerlings

d. Field Study

1. Type of Study: Clinical Field Trial

2. Name and Address of Investigator: R. T. Colesante
New York State Department of Environmental Conservation
Constantia, NY

3. General Design of the Study

a. Purpose of the Study: Evaluate the survival of walleye fry after oxytetracycline (OTC) marking and stocking in earthen ponds.

b. Test Animals: Walleye *(Stizostedion **vitreum)*** fry

c. Treatment Groups: Oxytetracycline-treated and untreated fry

d. Dosage Form: Water-soluble oxytetracycline hydrochloride

e. Route of Administration: Immersion (bath)

f. Dosages Used: 0 and 500 mg oxytetracycline/L of water for 6 hours

g. Test Duration: 45-55 days (treatment to harvest)

h. Variable: Survival was recorded.

4. Methods: In 1994, fry were immersed in a 500 mg/L oxytetracycline static bath for 6 hours or left untreated. Six ponds were stocked with marked fry and an additional six ponds were stocked with unmarked fry. Each pond was stocked with 20,000 fry. Ponds were harvested after 45-55 days.

5. Results: Survival results from each pond are shown in the following table.

Table 3.6. Survival results following otolith marking with oxytetracycline.

Pond No.	Treatment Group	Fry Stocked	Fingerling Return	
			Unmarked	Marked
1	OTC	20,000		22,728
2	OTC	20,000		15,557
3	OTC	20,000		11,347
4	Control	20,000	5,360	
5	Control	20,000	12,964	
6	OTC	20,000		14,118
7	Control	20,000	18,184	
8	OTC	20,000		13,432
9	Control	20,000	12,367	
10	Control	20,000	12,727	
11	Control	20,000	13,457	
12	OTC	20,000		11,697
Mean Survival			**62.5 %**	**74.1 %**

6. Conclusion: Based on this study, the recommended dose of oxytetracycline to achieve a fluorescent mark on the otolith, a six-hour immersion at 500 mg/L, is safe to walleye fry.

4. HUMAN SAFETY:

- **Toxicity:** An acceptable daily intake (ADI) of 25 micrograms per kilogram of body weight per day has been previously codified for total tetracycline residues (chlortetracycline, oxytetracycline, and tetracycline) (21 CFR 556.500).

- **Residue Depletion Studies:** Residue depletion data for fish marked with oxytetracycline have been summarized in PMF 5667 (67 FR 46527 dated July 15, 2002). The data are from PMF 3265 and the public literature. **A** discussion on the long inherent withdrawal period which occurs between treatment of the fish and possible consumption by humans also appears in PMF 5667. The data in PMF 5667 and the public literature, and the long inherent withdrawal period support the human food safety of the use of oxytetracycline to mark finfish fry and fingerlings.

- **Tolerance and Withdrawal Time:** A tolerance of 2 ppm in muscle tissue as the sum of tetracycline residues has been previously codified for the edible tissue of finfish (21 CFR 556.500). A withdrawal time beyond the grow-out period is not needed.

- **Microbial Food Safety:** The potential human health impact of the microbial effects associated with the use of oxytetracycline HCl to mark skeletal tissue, most often the otoliths, of finfish fry or fingerlings for subsequent identification, was assessed pursuant to CVM's Guidance for Industry #78 titled *Consideration of the Human Health Impact of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals.* The Agency has determined that use of oxytetracycline HCl as described in this application will not significantly impact the rate and extent of development of antimicrobial drug resistant enteric bacteria formed in the intestinal tract of treated fish following exposure to oxytetracycline HCl.

- **Regulatory Method for Residues:** The analytical method for detection of residues of oxytetracycline is a microbiological assay using *Bacillus cereus* var. *mycoides.* This method may be found in "Antibiotic Residues in Milk, Dairy Products, and Animal Tissues: Methods, Reports, and Protocols'' (revised October 1968, reprinted December 1974), National Center for Antibiotic and Insulin Analysis, FDA, Washington, DC 20204). The method is on file **at** the Center for Veterinary Medicine, 7500 Standish Pl., Rockville, MD 20855.

5. *AGENCY CONCLUSIONS:*

The data submitted in support of this ANADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations. The data demonstrate that OXYTETRACYCLINE HCL SOLUBLE POWDER-343, when administered by immersion at concentrations of 200 to 700 mg oxytetracycline hydrochloride/liter of water for 2 to 6 hours, is safe and effective to mark skeletal tissues of finfish fry and fingerlings as an aid in identification.

OXYTETRACYCLINE HCL SOLUBLE POWDER-343 for use in food-producing animals is currently marketed as an over-the-counter product. Adequate directions for safe and effective use by the layperson have been provided. Therefore, the Agency has concluded that this product may retain over-the-counter marketing status.

A tolerance of 2 ppm in muscle tissue as the sum of tetracycline residues has been previously codified for the edible tissue of finfish. A withdrawal time beyond the grow-out period is not needed. An ADI of 25 micrograms per kilogram of body weight per day has been previously codified for total tetracycline residues (chlortetracycline, oxytetracycline, and tetracycline). The potential human health impact of the microbial effects associated with the use of oxytetracycline hydrochloride to mark skeletal tissues of finfish as described in this document was assessed. The Agency has determined that use of oxytetracycline hydrochloride as described in this application will not significantly impact the rate and extent of development of antimicrobial drug resistant enteric bacteria formed in the intestinal tract of treated fish following exposure to oxytetracycline hydrochloride.

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this approval for food-producing animals does not qualify for marketing exclusivity.

In accordance with 21 CFR 514.106(b)(2)(vii), this is a Category II change involving the addition of a species and a new claim. The safety and effectiveness data in the parent application did not need to be reevaluated.

6. ATTACHMENTS:

Facsimile labeling is attached as indicated below:

OXYTETRACYCLINE HCL SOLUBLE POWDER-343 135.5 g (4.78 OZ)
OXYTETRACYCLINE HCL SOLUBLE POWDER-343 25 x 135.5 g (4.78 oz)
OXYTETRACYCLINE HCL SOLUBLE POWDER-343 272.2 g (9.6 oz)
OXYTETRACYCLINE HCL SOLUBLE POWDER-343 25 x 272.2 g (9.6 oz)

NDC 59130-704-78

OXYTETRACYCLINE HCl SOLUBLE POWDER-343

A broad spectrum ANTIBIOTIC

For control and treatment of specific diseases in poultry, cattle, sheep, swine and bees. For the marking of skeletal tissues in finfish fry and fingerlings as an aid in identification.

This packet contains 102.4 grams of oxytetracycline HCl

This packet will make:

512 gallons (1,938 L) containing 200 mg oxytetracycline HCl per gallon (equivalent to 52.8 mg/L)
256 gallons (969 L) containing 400 mg oxytetracycline HCl per gallon (equivalent to 105.6 mg/L)
128 gallons (484.5 L) containing 800 mg oxytetracycline HCl per gallon (equivalent to 211.4 mg/L)

For oral use only in poultry, cattle, sheep, swine and bees.

FOR ANIMAL USE ONLY

KEEP OUT OF REACH OF CHILDREN

NET WEIGHT: 135.5 g (4.78 oz)

ANADA 200-247, APPROVED BY FDA

AmTech® Group, Inc.

INDICATIONS AND DIRECTIONS FOR USE.

For the control of the following poultry diseases caused by organisms susceptible to oxytetracycline:Add the following amount to two gallons of stock solution when proportioner is set to meter at the rate of one ounce per gallon.

CHICKENS	DOSAGE	PACKETS/2 GALLONS STOCK SOLUTION
Infectious synovitis caused by *Mycoplasma synoviae*	200-400 mg/gal	1/2-1
Chronic respiratory disease (CRD) and air sac infection caused by *Mycoplasma gallisepticum* and *Escherichia coli*	400-800 mg/gal	1-2
Fowl cholera caused by *Pasteurella multocida*	400-800 mg/gal	1-2
TURKEYS		
Hexamitiasis caused by *Hexamita meleagridis*	200-400 mg/gal	1/2-1
Infectious synovitis caused by *Mycoplasma synoviae*	400 mg/gal	1
Growing Turkeys--Complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis)	25 mg/lb body weight daily	varies with age & water consumption (1 packet will treat 4,096 pounds of turkeys.)

Medicate continuously at the first clinical signs of disease and continue for 7 to 14 consecutive days. If improvement is not noted within 24-48 hours, consult a poultry diagnostic laboratory or poultry pathologist to determine diagnosis and advice on dosage.

For the control and treatment of the following diseases caused by organisms susceptible to oxytetracycline:

SWINE	DOSAGE
Bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* Bacterial pneumonia *caused* by *Pasteurella multocida* For Breeding Swine: Leptospirosis (reducing the incidence of abortions and shedding of leptospira) caused by *Leptospira pomona*.	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily. Administer up to 14 days.
CALVES, BEEF CATTLE AND NON-LACTATING DAIRY CATTLE	
Bacterial enteritis caused by *Escherichia coli* Bacterial pneumonia (shipping fever complex) *caused* by *Pasteurella multocida*.	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily. Administer up to 14 days.
SHEEP	
Bacterial enteritis caused by *Escherichia coli* Bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida*.	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily. Administer up to 14 days.

This packet will treat 10,240 pounds of swine, cattle or sheep at 10 mg/pound.

CAUTION: Use as sole source of oxytetracycline. Prepare fresh solutions every 24 hours.
Special Note: The concentration of drug required in medicated water must be adequate to compensate for variation in the age of the animal, feed consumption rate and the environmental temperature and humidity, each of which affects water consumption.

HONEY BEES	
American and European Foulbrood caused by *Bacillus larvae*, susceptible to oxytetracycline.	200mg/colony Administer in 3 applications of sugar syrup or 3 dustings at 4- to 5-day intervals. The drug should be fed early in the spring or fall and consumed by the bees before the main honey flow begins to avoid contamination of production honey.
FISH	
For the marking of skeletal tissues in finfish fry and fingerlings as an aid in identification.	Immerse fry or fingerling finfish in 200 to 700 mg OTC (buffered)/liter of water for 2 - 6 hours. Solution should be tested on a small number of fish before full-scale use. Once mixed with water, solution should be used immediately.
ADVERSE REACTIONS: Oxytetracycline HCl will acidify the water. The pH should be maintained at an acceptable level for fish by the addition of a buffer. Monitor water quality and temperature.	DISPOSAL OF TREATED WATER: Do not discharge marking immersion water containing oxytetracycline into surface waters.

RESIDUE WARNING: Do not administer to turkeys, cattle or sheep within 5 days of slaughter. Zero-day slaughter withdrawal in swine. Do not administer tu chickens or turkeys producing eggs for human consumption. Do not administer this product with milk or milk replacers. Administer 1 hour before or 2 hours after feeding milk or milk replacers.
A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal. A milk discard period has not been established for this product in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older. An additional withdrawal time beyond the grow-out period is not needed for fish.

RECOMMENDED STORAGE: STORE BELOW 77°F (25°C)
FOR USE IN DRINKING WATER ONLY
NOT FOR USE IN LIQUID FEED SUPPLEMENTS
FOR ANIMAL USE **ONLY.** KEEP OUT **OF REACH OF CHILDREN**
Restricted Drug(s) (California). Not For Human Use. Use Only As Directed.

Manufactured by
Phoenix Scientific, Inc.
St. Joseph, MO 64503

800507
Rev. 4-04

AmTech® is a registered trademark of Phoenix Scientific, Inc.

TAKE TIME OBSERVE LABEL DIRECTIONS

Lot No.

Exp. Date

3 59130 70478 5

NDC59130-704-78

OXYTETRACYCLINE HCl SOLUBLE POWDER-343

A broad *spectrum* ANTIBIOTIC

For control and treatment of specific diseases in poultry, cattle, sheep, swine and bees.
For the marking of skeletal tissues in finfish fry and fingerlings as an aid in identification.
Each packet contains 102.4 grams of oxytetracycline HCl.
Each packet will make: 512 gallons (1,938 L) containing 200 mg oxytetracycline HCl per gallon; (equivalent to 52.8 mg/L) 256 gallons (969 L) containing 400 mg oxytetracycline HCl per gallon; (equivalent to 105.7 mg/L) 128 gallons (484.5 L) containing 800 mg oxytetracycline HCl per gallon. (equivalent to 211.4mg/L).

INDICATIONS AND DIRECTIONS FOR USE

For the control of the following poultry diseases caused by organisms susceptible to oxytetracycline: Add the following amount to two gallons of stock solution when proportioner is set to meter at the rate of one ounce per gallon.

CHICKENS	DOSAGE	PACKS/2 GALLONS STOCK SOLUTION
Infectious synovitis caused by *Mycoplasma synoviae*	200-400 mg/gal	½ - 1
Chronic respiratory disease (CRD) and air sac infection caused by *Mycoplasma gallisepticum* and *Escherichia coli*	400-800 mg/gal	1 - 2
Fowl cholera caused by *Pasteurella multocida*	400-800 mg/gal	1 - 2
TURKEYS		
Hexamitiasis caused by *Hexamita meleagridis*	200-400 mg/gal	½ - 1
Infectious synovitis caused by *Mycoplasma synoviae*	400 mg/gal	1
Growing Turkeys-Complicating bacterial organisms associated with bluecomb (transmissible enteritis, coronaviral enteritis)	25 mg/lb body weight daily	varies with age & water consumption (1 packet will treat 4,096 pounds of turkeys.)

Medicate continuously at the first clinical signs of disease and continue for 7 to 14 consecutive days. If improvement is not noted within 24-48 hours, consult a poultry diagnostic laboratory or poultry pathologist to determine diagnosis and advice on dosage.

For the control and treatment of the following diseases caused by organisms susceptible to oxytetracycline:

SWINE Bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* Bacterial pneumonia caused by *Pasteurella multocida* For Breeding Swine: Leptospirosis (reducing the incidence of abortions and shedding of leptospira) caused by *Leptospira pomona*	**DOSAGE** Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily. Administer up to 14 days.
CALVES, BEEF CATTLE AND NON-LACTATING DAIRY CATTLE Bacterial enteritis caused by *Escherichia coli* Bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida*	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily. Administer up to 14 days.
SHEEP Bacterial enteritis caused by *Escherichia coli* Bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida*	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily. Administer up to 14 days.

Each packet will treat 10,240 pounds of swine, cattle or sheep at 10 mg/pound.

CAUTION: Use as sole source of oxytetracycline. Prepare fresh solutions every 24 hours.
Special Note: The concentration of drug required in medicated water must be adequate to compensate for variation in the age of the animal, feed consumption rate and the environmental temperature and humidity, each of which affects water consumption.

HONEY BEES American and European Foulbrood caused by *Bacillus larvae* susceptible to oxytetracycline.	200 mg/colony Administer in 3 applications of sugar syrup or 3 dustings at 4- to 5-day intervals. The drug should be fed early in the spring or fall and consumed by the bees before the main honey flow begins to avoid contamination of production honey.
FISH For the marking of skeletal tissues in finfish fry and fingerlings as an aid in identification.	Immerse fry or fingerling finfish in 200 to 700 mg OTC (buffered)/liter of water for 2-6 hours. Solution should be tested on a small number of fish before full-scale use. Once mixed with water, solution should be used immediately.
DISPOSAL OF TREATED WATER: Do not discharge marking immersion water containing oxytetracycline into surface waters.	**ADVERSE REACTIONS:** Oxytetracycline HCl will acidify the water. The pH should be maintained at an acceptable level for fish by the addition of a buffer. Monitor water quality and temperature.

RESIDUE WARNING: Do not administer to turkeys, cattle or sheep within 5 days of slaughter. Zero-day slaughter withdrawal in swine. Do not administer to chickens or turkeys producing eggs for human consumption. Do not administer this product with milk or milk replacers. Administer 1 hour before or 2 hours after feeding milk or milk replacers. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal. A milk discard period has not been established for this product in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older. An additional withdrawal time beyond the grow-out period is not needed for fish.

RECOMMENDED STORAGE: STORE BELOW 77°F (25°C)

FOR USE IN DRINKING WATER ONLY NOT FOR USE IN LIQUID FEED SUPPLEMENTS

Restricted Drug(s) (California). Not For Human Use. Use Only As Directed.

For oral use only in poultry, cattle, sheep, swine and bees.

FOR ANIMAL USE ONLY KEEP OUT OF REACH OF CHILDREN

NET WEIGHT: 25 x 135.5 g (4.78 oz)

ANADA 200-247, APPROVED BY FDA

TAKE TIME — INGREDIENT LABEL DIRECTIONS

AmTech® is a registered trademark of Phoenix Scientific, Inc.

Manufactured by Phoenix Scientific, Inc. St. Joseph, MO 64503

800507 Rev. 4-04

Lot No.

Exp. Date

AmTech® Group, Inc

3 59130 20478 0

NDC 59130-704-27

OXYTETRACYCLINE HCl SOLUBLE POWDER-343

A broad spectrum ANTIBIOTIC

For control and treatment of specific diseases in pouttry, cattle, sheep, swine and bees. For the marking of skeletal tissues in finfish fry and fingerlings as an aid in identification.

This packet contains 204.8 grams of oxytetracycline HCl

This packet will make:

1,024 gallons (3,876 U containing 200 mg oxytetracycline HCl per gallon (equivalent to 52.8 mg/L)
512 gallons (1,938 U containing 400 mg oxytetracycline HCl per gallon (equivalent to 105.7 mg/L)
256 gallons (969 U containing 800 mg oxytetracycline HCl per gallon (equivalent to 211.4 mg/L)

For oral use only in **poultry, cattle, *sheep*, Swine and bees.**

FOR ANIMAL USE ONLY

KEEP OUT OF REACH OF CHILDREN

NET WEIGHT: 272.2 g (9.6 oz)

ANADA 200-247, APPROVED BY FDA

AmTech® Group, Inc.

INDICATIONS AND DIRECTIONS FOR USE

For the control of the following pouttry diseases caused by Organlsms susceptible to oxytetracycline: Add the following amount to two gallons of stock solution when proportioner is set to meter at the rate of one ounce per gallon.

	DOSAGE	PACKETS/2 GALLONS STOCK SOLUTION
CHICKENS		
Infectious synovitis caused by ***Mycoplasma synoviae***	200-400 mg/gal	1/4-1/2
Chronic respiratory disease (CRD) and air sac infection caused by ***Mycoplasma gallisepticum*** and ***Escherichia coli***	400-800 mg/gal	1/2-1
Fowl cholera caused by ***Pasteurella multocida***	400-800 mg/gal	1/2-1
TURKEYS		
Hexamitiasis caused by ***Hexamita meleagridis***	200-400 mg/gal	1/4-1/2
Infectious synovitis caused by ***Mycoplasma synoviae***	400 mg/gal	1/2
Crowing Turkeys--Complicating bacterial organisms associated with bluecomb (transmissible enteritis. coronaviral enteritis)	25 mg/lb body weight daily	varies with age & water consumption (1 packet will treat 8,192 pounds of turkeys.)

Medicate continuously at the first clinical signs of disease and continue for 7 to 14 consecutive day.. If improvement is not noted within 24-48 hours, consult a poultry diagnostic laboratory or poultry pathologist to determine diagnosis and advice on dosage.

For the control and treatment of the following diseases caused by organisms susceptible to oxytetracycline:

	DOSAGE
SWINE	
Bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis*	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily.
Bacterial pneumonia caused by *Pasteurella multocida*	Administer up to 14 days.
For Breeding Swine: Leptospirosis (reducing the incidence of abortions and shedding of leptospira) caused by *Leptospira pomona*.	
CALVES, BEEF CATTLE AND NON-LACTATING DAIRY CATTLE	
Bacterial enteritis caused by *Escherichia coli*.	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily.
Bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida*.	Administer up to 14 days.
SHEEP	
Bacterial enteritis caused by *Escherichia coli*.	Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily.
Bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida*.	Administer up to 14 days.

This packet will treat 20,480 pounds of swine, cattle or sheep at 10 mg/pound.

CAUTION: Use as sole source of oxytetracycline. Prepare fresh solutions every 24 hours.
Special Note: The concentration of drug required in medicated water must be adequate to compensate for variation in the age of the animal, feed consumption rate and the environmental temperature and humidity, each of which affects water consumption.

HONEY BEES	
American and European Foulbrood caused by *Bacillus larvae*, susceptible to oxytetracycline.	200 mg/colony Administer in 3 applications of sugar syrup or 3 dusings at 4- to 5-day intervals. The drug should be fed early in the spring or fall and consumed by the bees before the main honey flow begins to avoid contamination of production honey.
FISH	
For the marking of skeletal tissues in finfish fry and fingerlings as an aid in identification.	Immerse fry or fingerling finfish in 200 to 700 mg OTC (buffered)/liter of water for 2-6 hours. Solution should be tested on a small number of fish before full-scale use. Once mixed with water, solution should be used immediately.
ADVERSE REACTIONS	**DISPOSAL OF TREATED WATER:**
Oxytetracycline HCl will acidify the water. The pH should be maintained at an acceptable level for fish by the addition of a buffer. Monitor water quality and temperature.	Do *NOT* discharge marking immersion water containing oxytetracycline into surface waters.

RESIDUE WARNING: Do not administer to turkeys, cattle or sheep within 5 days of slaughter. Zero-day daughter withdrawal in swine. Do not administer to chickens or turkeys producing eggs for human consumption. Do not administer this product with milk or milk replacers. Administer 1 hour before or 2 hours after feeding milk or milk replacers
A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal. A milk discard period has not been established for this product in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older. An addiional withdrawal lime beyond the grow-out period is not needed for fish

RECOMMENDED STORAGE: STORE BELOW 77°F (25°C)

FOR USE IN DRINKING WATER ONLY

NOT FOR USE IN LIQUID FEED SUPPLEMENTS

FOR ANIMAL USE ONLY. KEEP OUT OF REACH OF CHILDREN

Restricted Drug(s) (California). Not For Human Use. Use Only As Directed.

800507

Rev. 4-04

Manufactured by
PhoenixScientific, Inc.
St. Joseph, MO 64503

Lot No.

Exp. Date

TAKE TIME OBSERVE LABEL DIRECTIONS

3 59130 70427 3

NDC 59130-704-27

OXYTETRACYCLINE HCl SOLUBLE POWDER-343

A broad spectrum ANTIBIOTIC

For control and treatment of specific diseases in poultry, cattle, sheep, swine and bees. For the marking of skeletal tissues in finfish fry and fingerlings as an aid in identification.

Each packet contains 204.8 grams of oxytetracycline HCl.

Each packet will make: 1,024 gallons (3,876 L) containing 200 mg oxytetracycline HCl per gallon; 512 gallons (1,938 L) containing 400 mg oxytetracycline HCl per gallon: 256 gallons (969 L) containing 800 mg oxytetracycline HCl per gallon.

INDICATIONS AND DIRECTIONS FOR USE

For the control of the following poultry diseases caused by organisms susceptible to oxytetracycline: Add the following amount to two gallons of stock solution when proportioner is set to meter at the rate of one ounce per gallon.

	DOSAGE	PACKS/2 GALLONS STOCK SOLUTION
CHICKENS		
Infectious synovitis caused by Mycoplasma *synoviae*	200-400 mg/gal	1/4 - 1/2
Chronic respiratory disease (CRD) and air sac infection caused by *Mycoplasma gallisepticum* and Escherichia coli	400-800 mg/gal	1/2 - 1
Fowl cholera caused by Pasteurella *multocida*	400-800 mg/gal	1/2 - 1
TURKEYS		
Hexamitiasis caused by *Hexamita meleagridis*	200-400 mg/gal	1/4 - 1/2
Infectious synovitis caused by Mycoplasma *synoviae*	400 mg/gal	1/2
Growing Turkeys-Complicating bacterial organisms associated with bluecornb (transmissible enteritis, coronaviral enteritis)	25 mg/lb body weight daily	vanes with age & water consumption (1 packet will treat 8,192 pounds of turkeys.)

Medicate continuously at the first clinical signs of disease and continue for 7 to 14 consecutive days. If improvement is not noted within 24-48 hours, consult a poultry diagnostic laboratory or poultry pathologist to determine diagnosis and advice on dosage.

For the control and treatment of the following diseases caused by organisms susceptible to oxytetracycline:

SWINE
Bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis*
Bacterial pneumonia caused by Pasteurella *multocida*
For Breeding Swine: Leptospirosis (reducing the incidence of abortions and shedding of leptospira) caused by *Leptospira pomona*.

DOSAGE
Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily. Administer up to 14 days

CALVES, BEEF CATTLE AND NON-LACTATING DAIRY CATTLE
Bacterial enteritis caused by *Escherichia* coli
Bacterial pneumonia (shipping fever complex) caused by Pasteurella *multocida*.

Administer in the drinking water at a level of 10 mg oxytetracycline HCl per pound of body weight daily. Administer up to 14 days

SHEEP
Bacterial enteritis caused by *Escherichia coli*
Bacterial pneumonia (shipping fever complex) caused by *Pasteurella multocida*.

Administer in the drinking water at a level of 10 mg oxytetracycline HCl pet pound of body weight daily. Administer up to 14 days.

Each packet will treat 20,480 pounds of swine. cattle or sheep at 10 mg/pound.

CAUTION; Use as sole source of oxytetracycline. Prepare fresh solutions every 24 hours.
Special Note: The concentration of drug required in medicated water must be adequate to compensate for variation in the age of the animal, feed consumption rate and the environmental temperature and humidity, *each* of which affects water consumption.

HONEYBEES
American and European Foulbrood caused by *Bacillus* larvae, susceptible to oxytetracycline.

200mg / colony
Administer in 3 applications of sugar syrup or 3 dustings at 4- to 5-day intervals. The drug should be fed early in the spring or fall and consumed by the bees before the main honey flow begins to avoid contamination of production honey.

FISH
For the marking of skeletal tissues in finfish fry and fingerlings as an aid in Identification.

Immerse fry or fingerling finfish in 200 to 700 mg OTC (buffered)/ liter of water for 2-6 hours. Solution should be tested on a small number of fish before full-scale use. Once mixed with water, solution should be used immediately.

ADVERSE REACTIONS:
Oxytetracycline HCl will acidify the water. The pH should be maintained at an acceptable level for fish by the addition of a buffer. Monitor water quality and temperature.

DISPOSAL OF TREATED WATER
Do not discharge marking immersion water containing oxytetracycline into surface waters.

WARNING: Do not administer to turkeys, cattle or sheep within 5 days of slaughter. Zero-day slaughter withdrawal in swine. Do not administer to chickens or turkeys producing eggs for human consumption. Do not administer this product with milk or milk replacers. Administer 1 how before or 2 hours after feedii milk or milk replacen. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal. A milk discard period has not been established for this product in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older. An additional withdrawal time beyond the grow-out period is not needed for fish.

RECOMMENDED STORAGE: STORE BELOW 77°F (25°C)

FOR USE IN DRINKING WATER ONLY NOT FOR USE IN LIQUID FEED SUPPLEMENTS

Restricted Drug(s) (California). Not For Human Use. Use Only As Directed.

For oral use only in poultry, cattle, *sheep*, swine and bees.

FOR ANIMAL USE ONLY KEEP OUT OF REACH OF CHILDREN

NET WEIGHT: 25 x 272.2 g (9.6 oz) ANADA 200-247, APPROVED BY FDA

800507 is a registered trademark of Phoenix Scientific, Inc. Rev. 4-04

Lot No.

Exp. Date

AmTech Group, Inc. ®

TAKE TIME OBSERVE LABEL DIRECTIONS

Manufactured by
Phoenix Scientific, Inc.
St. Joseph, MO 64503

30 204 78